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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,170	12/22/2003	Anke Esperester	01-1445	7746

28501 7590 03/26/2008

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EXAMINER	
LEITH, PATRICIA A	
ART UNIT	PAPER NUMBER
1655	

MAIL DATE	DELIVERY MODE
03/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/743,170	ESPERESTER ET AL.	
	Examiner	Art Unit	
	Patricia Leith	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-16 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-16 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/17/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4-16 and 29-31 are pending in the application and were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office Action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-16 and 29-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,991,816 (reference provided in the IDS submitted by Applicants on 12/17/07) in view of Struengmann (US 6,284,269) in view of Mathowitz, E. (1999) .

Bilgrami et al. did not specifically teach wherein the red vine leaf water extract was contained in a tablet with a disintegrant such as colloidal, anhydrous silica, a binder such as microcrystalline cellulose, a filler such as hydrogen phosphate or magnesium stearate, a plasticizer, a colorant or the particular amounts of each constituent in the tablet.

Struengmann (US 6,284,269) disclosed conventional tablet additives such as hydrogen phosphate, colloidal anhydrous silica, sodium starch, magnesium stearate, microcrystalline cellulose (see example V/7, col's 10-11) as well as plasticizers such as polyethylene glycol (see claim 10). Thus, it was known that all of the tablet ingredients as Instantly claimed were conventional tablet ingredients, known at the time the invention was made.

Mathowitz, E. (1999) disclosed the conventional practice of addition of controlled-release coatings (films) in tablet manufacture (see pages 302 and 306-309).

It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to determine all operable and optimal concentrations of components because concentration of aqueous red vine leaf extract is an art-recognized result-effective variable which would have been routinely determined and optimized in the pharmaceutical art. Although the prior art do not teach the particular combination of carriers which are added to the red vine extract or all the various permutations of concentration ranges as claimed, it would be conventional and within the skill of the art to identify the optional concentrations of a given excipient because (1) the selection of appropriate concentration of excipients to stabilize red vine extract for the intended purpose of preventing its denaturation and decomposition during storage are conventional and within the skill in the art, and (2) hydrogen phosphate, colloidal anhydrous silica, sodium starch, magnesium stearate, microcrystalline cellulose and polyethylene glycol are well known in the art as excipients to used for tableting active ingredients. The incorporation of known active ingredients into tablets with conventional carriers was well within the purview of the ordinary artisan at the time the invention was made, and is hence considered *prima facie* obvious.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-16 and 29-31 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bilgrami et al. (1993) in view of Struengmann (US 6,284,269) in

view of Mathowitz, E. (1999) for the reasons keenly set forth in the previous office action as well as any additional support indicated *infra.*

Applicants initially argue that the combination of references does not render the claimed invention obvious in that the prior art does not recite all of the claimed elements such as "a dried extract that consists essentially of ingredients of an aqueous extract of red vine leaves and up to about 10% by weight of colloidal, anhydrous silica" (see p. 7, remarks). In support thereof, Applicants state that "…the present invention...recites colloidal, anhydrous silica as a component of the dried extract *per se* rather than merely within or surrounding the tablet. The dried extract (including the silica) is a separate ingredient in the tablet apart from the excipient" (p. 7, remarks). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., The dried extract (including the silica) is a separate ingredient in the tablet apart from the excipient) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the combination does not teach or suggest a dried extract consisting of colloidal, anhydrous silica: "Bilgrami does not provide or even suggest a dried extract comprising silica. Struengmann discloses silica as a conventional tablet additive, but, like Bilgrami, also does not provide or even suggest a dried extract

comprising silica" (p. 8, remarks). In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

First, it is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision Ex parte Smith, --USPQ2d--, slip op. at 20 (Bd. Pat. App.& Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf). Second, it would have been obvious, based upon the cited prior art to combine the dried extract into a composition consisting of, or consisting essentially of or comprising colloidal, anhydrous silica because the extract was known to be medicinally active. The exclusion of water from the extract would have been clearly necessary to admix with binders/fillers in order to impart said extract into a medicinal form such as a tablet or capsule. The incorporation of a known, medicinal extract into known, conventional carriers to create pharmaceutical dosage forms is deemed *prima facie* obvious lacking any unexpected results. "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton *KSR* 127S. Ct. at 1742.

Claims 1, 7, 9, 13, 29 and 30 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Esperester et al. (WO 01/28363 A1) as provided in, and as necessitated by the IDS submitted by Applicants on 12/17/07.

Esperester et al. (WO 01/28363 A1) taught oral compositions such as capsules and tablets comprising an aqueous extract of red vine leaf for treatment of venous insufficiency:

> In a preferred embodiment, the dietary supplement is in a form suitable for oral administration, in particular in a solid dosage form, i.e. **a capsule or tablet, that consists of 20 to 60% of aqueous red vine leaf extract with a high flavonoid content of 2-15**%. Another preferred dosage form is that of drops containing 3 to 90% of extract. Further suitable administration forms may be coated tablets, syrups, or the like (see p. 3).... ..... **For the preparation of solid dosage forms the thick extract is dried, for instance by use of a vacuum drying oven or a vacuum drying conveyer. Carriers or excipients may be added during drying to facilitate further processing of the extract. Such carriers or excipients may be silicon dioxide, maltodextrine, glucose syrup, cellulose and others** (see paragraph bridging pp. 4-5, emphasis added).

It is noted that silicon dioxide is colloidal silica. Also, it is clear that because the carriers are added during drying, that the silica and other carriers are in dried form, and more than likely in powdered form even though the reference does not explicitly teach that the carriers are in powdered form.

It is apparent that Esperester et al. clearly taught drying of the extract prior to admixing into a tablet with a carrier such as silicon dioxide.

Also, please see claims 1-15 and especially claim 9 which states:

> 9. A method according to claim 8 wherein said red vine leaf extract is present within the range of 1 to 50% related to the total mass of the dietary supplement composition.

Esperester et al. did not specifically disclose an embodiment which included colloidal silica and an aqueous extract of red vine leaf in the claimed amounts.

Although Esperester et al. did not disclose an explicit embodiment which showed a tablet comprising the claimed amounts of red vine leaf aqueous extract and colloidal silica, Esperester et al. clearly strongly suggested such a combination in that they plainly taught that a capsule or tablet comprising 20-60% of red vine leaf aqueous extract was advantageously added to a carriers such as silicon dioxide (colloidal silica) to make into tablets/capsules.

Further, while Esperester et al. did not specifically teach the amounts of the silica (or cellulose) as Instantly claimed, it is clear that because the capsule or tablet contained from 20 to 60% of the active ingredient (i.e., the aqueous extract of red vine leaves) that the carrier could have been present in an amount from 40-80% of the tablet. Further, although Esperester et al. did not explicitly recite the amounts of silica (or cellulose) as Instantly claimed, it is deemed that the adjustment of concentration of the carrier with respect to the active ingredients and other suitable carriers would have

been well within the purview of the ordinary artisan at the time the invention was made because such adjustments were considered conventional in the art of pharmacology.

Claims 1, 4-16 and 29-31 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Esperester et al. (WO 01/28363 A1) in view of Bilgrami et al. (1993) in view of Struengmann (US 6,284,269) in view of Mathowitz, E. (1999).

The teachings of Esperester et al. were discussed above. The teachings of Esperester et al. did not specifically include wherein the tablet containing the aqueous extract of red vine leaves and a carrier such as silica or cellulose was coated with a film, or wherein the tablet specifically contained a binder, and a disintegrant, a lubricant and an excipient, magnesium stearate, a plasticizer, a colorant or the particular amounts of each constituent as Instantly claimed.

Bilgrami et al. (1993) studied the preventative effects of aqueous *Vitis vinefera* L. leaf. (red vine leaf) on nephrotoxicosis due to ingestion of the micotoxin citrinin. Bilgrami et al. discovered that *V. vinefera* L. leaf water extract administered by intubation to albino Swiss mice challenged with citrinin possessed greater toxicity prevention than cortisone (see entire reference, especially Table 1 and p. 482, col. 2).

Struengmann (US 6,284,269) disclosed conventional tablet additives such as hydrogen phosphate, colloidal anhydrous silica, sodium starch, magnesium stearate,

microcrystalline cellulose (see example V/7, col's 10-11) as well as plasticizers such as polyethylene glycol (see claim 10). Thus, it was known that all of the tablet ingredients as Instantly claimed were conventional tablet ingredients, known at the time the invention was made.

Mathowitz, E. (1999) disclosed the conventional practice of addition of controlled-release coatings (films) in tablet manufacture (see pages 302 and 306-309).

It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to determine all operable and optimal concentrations of aqueous red vine leaf extract because this extract is an art-recognized result-effective variable (i.e., having an advantageous effect on venous insufficiency) which would have been routinely determined and optimized in the pharmaceutical art. Although the prior art do not teach the particular combination of carriers which are added to the red vine extract or all the various permutations of concentration ranges as claimed, it would be conventional and within the skill of the art to identify the claimed concentrations of given excipients because (1) the selection of appropriate concentration of excipients to stabilize red vine extract for the intended purpose of preventing its denaturation and decomposition during storage are

conventional and within the skill in the art, and (2) hydrogen phosphate, colloidal anhydrous silica, sodium starch, magnesium stearate, microcrystalline cellulose and polyethylene glycol are well known in the art as excipients to used for tableting active ingredients. The incorporation of known active ingredients into tablets with conventional carriers was well within the purview of the ordinary artisan at the time the invention was made, and is hence considered *prima facie* obvious.

It would have further been obvious to create a tablet comprising aqueous red vine leaf extract with an enteric coating in order to shield the active ingredients of the extract from the acidic environment of the stomach in order to allow the active ingredients to pass undestructed into the small intestine for absorption into the bloodstream. It is clear from the teachings of Bilgrami et al. that the active ingredients enter into the bloodstream. Therefore, one of ordinary skill in the art would have easily recognized that protection of the extract would have been advantageous in order to prevent the degradation of the active components in order to optimize the effectiveness of the medicinal extract.

It is deemed that the claimed invention is an obvious variant of the compositions disclosed by Esperester et al. and/or Bilgrami et al. respectively and is thus unpatentable. The carriers which are added to the known, medicinal product of an aqueous extract of red vine leaf were well-known in the art as conventional tableting excipients and thus, the addition of such known excipients and concentration

adjustment thereof is deemed plainly obvious to one of ordinary skill in the art of pharmaceutical compounding. [If]… there are [a] finite number of identified, predictable solutions, [a] person of ordinary skill in art has good reason to pursue known options within his or her technical grasp, and if this leads to anticipated success, it is likely product of ordinary skill and common sense, not innovation *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 U.S. 2007. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 12/17/07 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patricia Leith
Primary Examiner
Art Unit 1655

February 28, 2008

/Patricia Leith/

Primary Examiner, Art Unit 1655